



Appendix C

Clean Copy of All Claims Pending After Entrance of the Present Amendment

1. A method for the combinatorial biosynthesis of one or more compounds comprising:
 - a) providing one or more starter units, wherein said one or more starter units have incorporated therein a functional handle that reacts with a functionality present on a solid support unit, the starter units being accepted as substrates for one or more modular biosynthetic enzymatic machinery systems;
 - b) attaching said one or more starter units to a solid support unit to provide one or more support bound starter units;
 - c) providing said one or more support bound starter units to said one or more biosynthetic enzymatic machinery systems to generate a collection of template structures;
 - d) functionalizing said template structures using synthetic organic chemistry; and
 - e) repeating steps c) and/or d) until a desired support bound collection of structures is generated.
2. The method of claim 1 further comprising functionalizing said support bound collection of structures generated in step e) to provide a support bound collection of unnatural natural products.
3. A method for the combinatorial biosynthesis of one or more compounds comprising:
 - a) providing one or more starter units, wherein said one or more starter units have incorporated therein a functional handle that reacts with a functionality present on a solid support unit, the starter units being accepted as substrates for one or more modular biosynthetic enzymatic machinery systems;
 - b) attaching said one or more starter units to a solid support unit to provide one or more support bound starter units;

- c) providing said one or more support bound starter units to said one or more biosynthetic enzymatic machinery systems to generate a collection of template structures; and
- d) functionalizing said collection of structures to provide a support bound collection of unnatural natural products.

5. The method of claim 1 further comprising the step of cleaving said support bound collection of structures from said solid support unit.

6. The method of claim 2 or 3 further comprising the step of cleaving said support bound collection of unnatural natural products from said solid support unit.

7. The method of claim 1, 2 or 3 wherein the functional handle is a chemically robust functionality, which includes an alkyne, an olefin or an iodoalkene.

8. The method of claim 1, 2 or 3 wherein the step of attaching the starter units to the solid support unit is effected by a chemical reaction which includes Glaser coupling, olefin metathesis or Stille coupling reaction.

9. The method of claim 1, 2 or 3 wherein the biosynthetic enzymatic machinery systems comprise one or more naturally-occurring synthetic enzymes.

10. The method of claim 9 wherein the biosynthetic enzymatic machinery systems comprise one or more enzymes which include fatty acid synthase, polyketide synthase, peptide synthase or terpene (or isoprenoid) synthase.

11. The method of claim 1, 2 or 3 wherein the biosynthetic enzymatic machinery systems comprise one or more modified enzymes.

12. The method of claim 11 wherein the modified enzyme is a genetically modified enzyme.
13. The method of claim 11 wherein the modified enzyme is a class I polyketide synthase enzyme.
14. The method of claim 1, 2 or 3 wherein the structure of one or more starter units incorporates an antibody recognition element.
15. The method of claim 1, 2 or 3 wherein one or more template structures incorporate an antibody recognition element.
16. The method of claim 1, 2 or 3 wherein the step of functionalizing said template structures is carried out using combinatorial techniques including, but not limited to, parallel synthesis and split-and-pool synthesis.
17. The method of claim 1, 2 or 3 wherein the step of functionalizing the template structures includes attaching a biomolecule to said template structures.
18. The method of claim 17 wherein the biomolecule includes polysaccharides, nucleic acids, peptides, and polymers.
19. The method of claim 1, 2 or 3 further comprising the step of recording the reaction history using an encoding technique.
20. The method of claim 19 wherein the encoding technique is selected from the group consisting of spatial encoding techniques, graphical encoding techniques, chemical encoding techniques and spectrometric encoding techniques.

21. The method of claim 20 wherein the spectrometric encoding technique is selected from the group consisting of mass spectroscopy, fluorescence emission and nuclear magnetic resonance spectroscopy.